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**Evaluation of Insulin Resistance in Severe Preeclampsia.**

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**Abstract:**

**Introduction:** the cause of preeclampsia has not been precisely understood. One of the reasons, as stated by some, might be resistance to insulin however, the role of insulin resistance in occurrence of preeclampsia has not been proven so far. Hence, the objective of this study is to find out the relationship between insulin resistance and severe preeclampsia.

**Materials and Methods:** In this case-control study 26 healthy pregnant women and 26 women with severe preeclampsia, for whom termination of pregnancy was concluded, were included. Both groups in terms of age, weight, parity and body mass index (BMI) were identical. Furthermore, FBS level, fasting blood insulin and resistance to insulin at the same laboratory and by similar procedures were evaluated for both groups throughout the study and documented in relevant forms. The data were analyzed by SPSS software and P value <0.05 was considered significant.

**Results:** The results showed that the level of FBS was not significantly different in preeclamptic patients and healthy pregnant control ( $p=0.062$ ). Moreover we found that the levels of fasting insulin was similar within two groups ( $P=0.80$ ).

**Conclusion:** In current study no relevant was observed between severe preeclampsia and resistance to insulin.

**Keywords: Preeclampsia; Insulin resistance; Blood pressure disorders; Pregnancy**

**Introduction:**

Blood pressure disorders during pregnancy are common complaint and along with infection as well as hemorrhage together form a fatal triad leading to most of mortality and disability connected to pregnancy amongst mothers and fetuses.

According to a declaration by National Centre for Health Statistics in 2001; hypertension during pregnancy has been detected in 3.7% of all pregnancies and still it is considered as one of the most serious threat to the mothers.<sup>(1)</sup>

In spite of its importance which led to decades of thorough research, yet the commencement and enhancement of hypertension in connection to pregnancy remains obscure and blood pressure disorder is one of the unresolved problems in maternity medicine although the consequences of hypertension have been explained long ago.<sup>(2)</sup> Even so, widespread researches are now being carried out but, regretfully the main causes for this disorder have not been specifically determined so far.

On the other hand, resistance to insulin is attributed to a situation when the ratio of FBS to fasting blood insulin is less than 4.5.<sup>(3,4)</sup> Although, according to some records a remarkable number of patients suffering from hypertension do show resistance to insulin and bear higher level of insulin but the causes for these two phenomena remain indefinite.<sup>(5)</sup>

In a study, it has been affirmed that; women who have been affected by preeclampsia have partly shown resistance to insulin and afterward it has been sug-

gested that women with pregnancy diabetes are critically prone to severe preeclampsia.<sup>(6)</sup> Similarly in another document no association between resistance to insulin, which happens during the third trimester of pregnancy, and hypertension has been confirmed and the former has been regarded as a phenomenon connected to all pregnancies that takes place during the third trimester.<sup>(7)</sup> Nevertheless, none of the broad researches so far have reached to an explicit conclusion in this regard though, different studies have stressed on an association between the markers of resistance to insulin and high blood pressure during pregnancy but still more data is required to prove that whether resistance to insulin does play a critical role in occurrence of high blood pressure during pregnancy or not? In order to fulfill such objectives more prospective studies in long term seem mandatory.<sup>(2)</sup>

That's why; preeclampsia is taken into account as one of the frequent diseases during pregnancy that could lead to serious outcomes including death. Hence, identification of causative agent for this phenomenon seems quite vital that might help in taking preventive measures. Above stated reasons persuaded us to investigate insulin resistance in women affected by preeclampsia who had referred to Imam-Ali general hospital of Zahedan in comparison to control group. The latter may contribute in solution of this dreadful disorder.

**Materials and Methods:**

This case-control study was conducted during 2007 and cases were chosen

amongst pregnant women who had referred to maternity ward of Imam-Ali general hospital of Zahedan. Inclusion criteria were as: monocyesis, age between 15-25 years, parity zero and one, pregnancy time-span at term (more than full 37 weeks), FBS in first check up less than 95 mg/dl and having no past history of any chronic disease. The latter included: apparent diabetes, renal disorders, hypertension, cardiac ischemia, any lipid ailment, BMI prior to pregnancy less than 25 kg/m<sup>2</sup> and lack of any medication except standard ones prescribed during pregnancy. Besides, nonexistence of apparent diabetes within closes family and last but not least absence of proteinuria or urinary tract infection during pregnancy. After thorough consideration of above mentioned criteria a group of 26 patients suffering from acute preeclampsia were chosen as test individuals.

This study was approved by ethical committee of Zahedan University of Medical Sciences and informed consent was taken from case and control groups. Fasting blood sample was collected exactly eight hours after labor. The sera were separated after centrifugation of the specimens and sent to laboratory for measurement of FBS and insulin. Blood sugar was measured by commercial available kit using autoanalyzer RA-1000 apparatus. Insulin was determined by commercial sandwich ELISA Kit. Insulin resistance determined using HOMA score (serum Insulin ( $\mu$ IU/ml)  $\times$  FBS (mg/dl) /405)

Data were expressed as Mean  $\pm$  SD and analyzed by SPSS software using un-

paired T-test and P value less than 0.05 was considered statistically significant.

### Results:

The study groups had similar age, BMI, and gestational age, whereas systolic and diastolic blood pressure values were significantly higher in the preeclamptic group than in healthy pregnant (table 1). We determined FBS and insulin levels in case and control group. As shown in table 1 FBS and insulin levels were not different significantly between the groups.

Finally, resistance to insulin, the main objective, of this study was taken into account between both groups. Optimal ratio in women with normal pregnancy was 156 (SD=269) whilst this ratio within those affected by severe preeclampsia was 191 (SD=283) and P value was 0.59 so, this comparison too was irrelevant.

As a result, indices extracted from this study as: BMI, FBS, fasting insulin and resistance to insulin with probability level of 95% were all insignificant since, t was  $>2$  and P value in all cases was  $>0.05$  so that, in this study no relevance between preeclampsia and resistance to insulin was observed (Table 1).

### Discussion:

In this case-control study of previously healthy women, we found that the insulin resistance did not have statistical significance in preeclamptic and normotensive women at term gestational age.

The researchers, who had separately carried out investigations concerning level of insulin, sensitivity or resistance

to insulin in preeclampsia, had also stated that pathophysiology of preeclampsia has no relationship to insulin

resistance whatsoever; the latter finding corresponds to our study.<sup>(7- 10)</sup>

Table1, the comparison of measured indices between both groups

Compared indices	Control group	Case group	P value
Age (year)	20.27 ± 3.07	20.92 ± 3.45	0.47
BMI (kg/m <sup>2</sup> )	21.43 ± 3.88	21.25 ± 4.23	0.84
fasting blood sugar (mg/dl)	88.31 ± 13.04	90.50 ± 17.73	0.62
Fasting blood insulin (µIU/ml)	3.42 ± 3.27	3.13 ± 6.63	0.80
Insulin resistance (HOMA score)	0.76±0.7	0.46±0.45	0.72
Systolic blood pressure (mm Hg)	114 ± 3	158 ± 4	<.001
Diastolic blood pressure (mm Hg)	74 ± 7	110 ± 7	<.001

In another study carried out by Thadhani et al., 2004; they too assessed role of resistance to insulin in occurrence of preeclampsia. The later study was designed as prospective case-control in which 28 individuals were chosen as case group and 57 as controls. In twelfth week of their pregnancy the level of sex hormone bound to globulin (SHBG) in their sera was measured and it was revealed that in case group, who were then affected by preeclampsia, had lower level of SHBG. They had later concluded that preeclampsia was the cause for resistance to insulin but due to some limitations and restrictions in their study, they had stressed the need for more comprehensive study.<sup>(11)</sup>

In similar investigation insulin resistance syndrome was considered as a disease effective against vascular disorders and since preeclampsia too is responsible for deterioration of vascular system along with metabolic changes, so it was concluded that these two phenomena are somewhat related.<sup>(12)</sup>

In another study (1995), through examination of 13 sufferers of preeclampsia and another 13 normal pregnant women acknowledged that resistance to insulin and increase in insulin level is more amongst preeclamptic women than normal cases. They conducted their study two months after labor by administration of 75 grams of oral glucose.<sup>(13)</sup>

It has been shown that preeclampsia have a weakly association to insulin resistance.<sup>(14)</sup> If the latter hypothesis is proved, it can facilitate prevention of hypertension but this needs more work out.

Some other investigations have also put forward that resistance to insulin plays an important role in occurrence of preeclampsia, in their studies resistance to insulin has been evaluated on the basis of glucose tolerance test.<sup>(15, 16)</sup> However, in our survey glucose and insulin of fasting blood have been taken into account.

Nonetheless, according to the controversial results extracted from different research papers it seems that analyses of different causes are crucial. However, our

study demonstrated that there was no link between resistance to insulin and preeclampsia therefore, it is possible that episode of hypertension taking place during preeclampsia be indicative of disarray in state of equilibrium of blood pressure and has nothing to do with resistance to insulin.

As noted earlier; ambiguity in results obtained in different studies plus restrictions in each and every investigation necessitates more comprehensive research projects to be performed to answer the relevant questions. Since, preeclampsia is considered as one of the most crucial events during pregnancy that could lead to appalling circumstances therefore, exploration for finding the cause of this phenomenon can create valuable progress in prevention and cure of diseased women.

In conclusion, we found that there is no insulin resistance in preeclampsia. We recommend carrying out further investigations with prospective design and assessing insulin resistance calculating the homeostasis model assessment during all the pregnancy period to evaluate this possible association.

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